# PROPOSITION 65

# PROCESS FOR DEVELOPING SAFE HARBOR NUMBERS

**February 2001**

**Reproductive and Cancer Hazard Assessment Section**
**Office of Environmental Health Hazard Assessment**
**California Environmental Protection Agency**

*The energy challenge facing California is real. Every Californian needs to take immediate action to reduce energy consumption.*

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# Proposition 65 Safe Harbor Development

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency is the lead agency for the implementation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65 or the Act). In that role, OEHHA has developed Proposition 65 safe harbor levels -- no significant risk levels (NSRLs) for carcinogens and maximum allowable daily levels (MADLs) for chemicals that cause reproductive toxicity. The NSRL is the daily intake level calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime exposure at the level in question. The MADL is the highest level at which the chemical would have no observable adverse reproductive effect assuming exposure at 1,000 times that level. The NSRLs and MADLs are promulgated in Title 22, California Code of Regulations (CCR), Sections 12705 and 12805 respectively to assist interested parties in determining whether warnings are required for exposures to listed chemicals, and whether discharges of that chemical to sources of drinking water are prohibited. If an exposure subject to the Act can be shown to be less than the specific regulatory level, the responsible person has "safe harbor" from the warning requirement and discharge prohibition. The availability of a safe harbor level provides greater certainty to responsible parties in complying with the Act and to the public in determining which exposures and discharges are of concern.

A three-tiered process for development of NSRLs is currently in place. NSRLs may be based on:

- *de novo* dose response assessments conducted or reviewed by OEHHA (22 CCR §12705(b))
- assessments conducted by another state or federal agency (22 CCR §12705(c)), or
- expedited assessments conducted by OEHHA (22 CCR §12705(d)).

The process for development of MADLs is described in 22 CCR §12803. Further specification of procedures used and assumptions made in developing safe harbor numbers are set out in regulation (See Appendix I).

As noted above, safe harbor levels may be based on risk assessments conducted outside OEHHA. In some cases, this can expedite safe harbor development. However, it should be noted that the process of review and consideration of existing assessments can be a lengthy one, and will depend on the complexity of the scientific information underlying the assessment, as well as on available resources.

OEHHA is committed to developing 20-35 safe harbor levels per year, using the processes described above. The needs of the regulated community and the public are important in selecting chemicals for safe harbor development. Any interested party wishing to have a specific chemical assessed should make that request in writing and provide a rationale for why the assessment of that chemical is needed. The contact for such submissions is: Ms. Cynthia Oshita, California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, P.O. Box 4010, Sacramento,

California 95812-4010. Ms. Oshita's telephone number is (916) 445-6900, and fax number is (916) 323-8803.

Some of the factors OEHHA considers in ordering chemicals for safe harbor development include the availability of dose response data, public input, and resources required to perform any particular dose response assessment. In accordance with the settlement agreement in the case of AFL-CIO et al. v. Deukmejian (Sacramento Superior Court No. 3481295), priority lists for development of safe harbor levels (i.e., NSRLs) were periodically released (OEHHA, 1993, 1994, 2000). The current *Status Report* (OEHHA, 2001) on the development of safe harbor levels for Proposition 65 listed chemicals is comprised of the following tables:

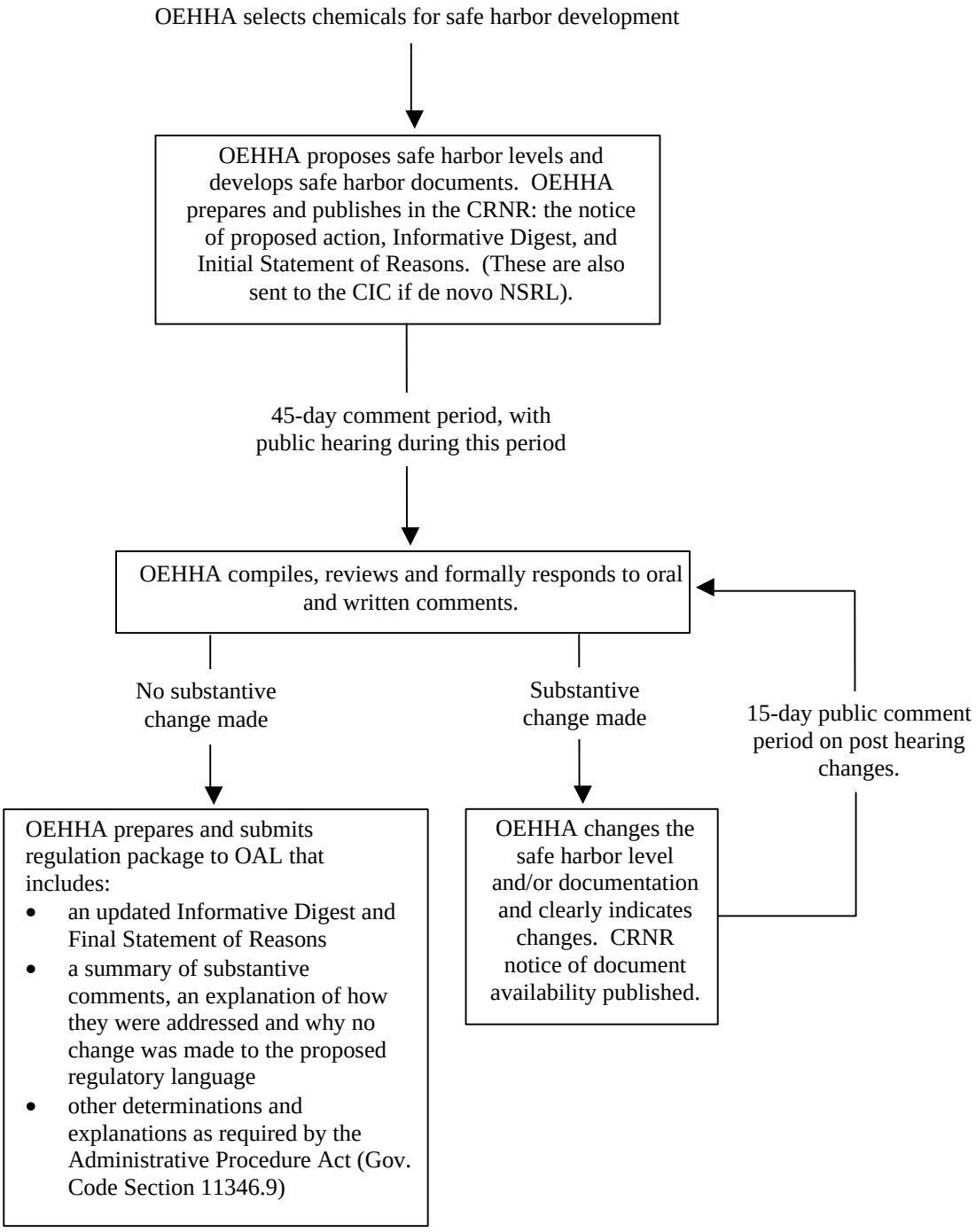
Table A -- a list of NSRLs adopted in regulation for carcinogens (22 CCR §12705),
Table B -- a list of MADLs adopted in regulation for chemicals causing reproductive toxicity (22 CCR §12805),
Table C -- a priority list for the development of NSRLs, and
Table D -- a priority list for the development of MADLs.

The listing of the chemicals in Tables C and D is based on the speed with which OEHHA anticipates completion of the NSRLs or MADLs given data availability, along with public input, resources, and priorities in the settlement agreement. The current *Status Report* is available from the OEHHA web site (www.oehha.ca.gov) and Ms. Oshita at the address given for her above.

Pursuant to the settlement agreement, OEHHA plans to routinely release an updated priority list. OEHHA intends this program to assist businesses with compliance with Proposition 65.

Regulatory guidance for the process by which safe harbor levels are developed is provided in 22 CCR Sections 12701-12705 and 12801-12803 and the Administrative Procedure Act (Government Code Section 11340 *et seq.*), as summarized in Figure 1.

**Figure 1. Safe Harbor Development.**




CIC: Carcinogen Identification Committee
NSRL: No Significant Risk Level

## References

American Federation of Labor and Congress of Industrial Organizations, the Natural Defense Council, Environmental Defense Fund, Sierra Club, Public Citizen, Inc., Campaign California, Citizens for a Better Environment, Silicon Valley Toxics Coalition, Bernardo Huerta v. Deukmejian. Settlement Agreement. Sacramento Superior Court No. 3481295. 1992.

Office of Environmental Health Hazard Assessment (OEHHA, 1993). Priority List for the Development of Carcinogen Dose Response Assessment for Proposition 65. OEHHA, Sacramento, CA, January 1993.

Office of Environmental Health Hazard Assessment (OEHHA, 1994). Safe Drinking Water and Toxic Enforcement Act of 1986 (Prop. 65). No Significant Risk Levels for Carcinogens. Acceptable Intake Levels for Reproductive Toxicants. Status Report. Part C, OEHHA, Sacramento, CA, January 1994.

Office of Environmental Health Hazard Assessment (OEHHA, 2000). Appendix II: Status Report: No Significant Risk Levels for Carcinogens and Maximum Allowable Daily Levels for Chemicals Causing Reproductive Toxicity. In: OEHHA, Proposition 65 Background Document. Public Workshop on Developing Safe Harbor Numbers, OEHHA, Sacramento, CA, October.

Office of Environmental Health Hazard Assessment (OEHHA, 2001). Status Report: No Significant Risk Levels for Carcinogens and Maximum Allowable Daily Levels for Chemicals Causing Reproductive Toxicity. OEHHA, Sacramento, CA, February.

# APPENDIX I
# Proposition 65 Regulations Governing the Development of Safe Harbor Levels

## TITLE 22. Chapter 3. Safe Drinking Water and Toxic Enforcement Act of 1986

### Article 7. No Significant Risk Levels

§12701. General.

(a) The determination of whether a level of exposure to a chemical known to the state to cause cancer poses no significant risk for purpose of Health and Safety Code Section 25249.10(c) shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of the chemical as known to the state to cause cancer. Nothing in this article shall preclude a person from using evidence, standards, risk assessment methodologies, principles, assumptions or levels not described in this article to establish that a level of exposure to a listed chemical poses no significant risk.

(b) A level of exposure to a listed chemical, assuming daily exposure at that level, shall be deemed to pose no significant risk provided that the level is determined:
  (1) By means of a quantitative risk assessment that meets the standards described in Section 12703,
  (2) By application of Section 12707 (Routes of Exposure); or
  (3) By one of the following, as applicable:
    (A) If a specific regulatory level has been established for the chemical in question in Section 12705, by application of that level.
    (B) If no specific level is established for the chemical in question in Section 12705, by application of Section 12709 (Exposure to Trace Elements) or 12711 (Levels Based on State or Federal Standards) unless otherwise provided.

(c) The chemicals, routes of exposure and conditions of use specifically listed in this article do not include all chemicals, routes of exposure and conditions of use that pose no significant risk. The fact that a chemical, route of exposure or condition of use does not appear in this article does not mean that it poses a significant risk.

(d) This article establishes exposure levels posing no significant risk solely for purposes of Health and Safety Code Section 25249.10(c). Nothing in this article shall be construed to establish exposure or risk levels for other regulatory purposes.

§12703. Quantitative Risk Assessment.

(a) A quantitative risk assessment which conforms to this section shall be deemed to determine the level of exposure to a listed chemical which, assuming daily exposure at that level, poses no significant risk. The assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause cancer. In the absence of principles or assumptions scientifically more appropriate, based upon the available data, the following default principles and assumptions shall apply in any such assessment:
  (1) Animal bioassay studies for quantitative risk assessment shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, the route of exposure, and the extent of tumor occurrence.
  (2) The quality and suitability of available epidemiologic data shall be appraised to determine whether the study is appropriate as the basis of a quantitative risk assessment, considering such factors as the selection of the exposed and reference groups, reliable ascertainment of exposure, and completeness of follow-up. Biases and confounding factors shall be identified and quantified.

(3) Risk analysis shall be based on the most sensitive study deemed to be of sufficient quality.
(4) The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.
(5) The absence of a carcinogenic threshold dose shall be assumed and no-threshold models shall be utilized. A linearized multistage model for extrapolation from high to low doses, with the upper 95 percent confidence limit of the linear term expressing the upper bound of potency shall be utilized. Time-to-tumor models may be appropriate where data are available on the time of appearance of individual tumors, and particularly when survival is poor due to competing toxicity.
(6) Human cancer potency shall be derived from data on human or animal cancer potency. Potency shall be expressed in reciprocal milligrams of chemical per kilogram of bodyweight per day. Interspecies conversion of animal cancer potency to human cancer potency shall be determined by multiplying by a surface area scaling factor equivalent to the ratio of human to animal bodyweight, taken to the one-third power. This is equivalent to a scaling factor of 14 when extrapolating from mouse data, and a scaling factor of 6.5 when extrapolating from rat data.
(7) When available data are of such quality that physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the risk assessment for inter-species, inter-dose, and inter-route extrapolations.
(8) When the cancer risk applies to the general population, human body weight of 70 kilograms shall be assumed. When the cancer risk applies to a certain subpopulation, the following assumptions shall be made, as appropriate:

| Subpopulation | Kilograms of Body Weight |
|---|---|
| Man (18+ years of age) | 70 |
| Woman (18+ years of age) | 58 |
| Woman with conceptus | 58 |
| Adolescent (11-18 years of age) | 40 |
| Child (2-10 years of age) | 20 |
| Infant (0-2 years of age) | 10 |

(b) For chemicals assessed in accordance with this section, the risk level which represents no significant risk shall be one which is calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime exposure at the level in question, except where sound considerations of public health support an alternative level, as, for example:
(1) where chemicals in food are produced by cooking necessary to render the food palatable or to avoid microbiological contamination; or
(2) where chlorine disinfection in compliance with all applicable state and federal safety standards is necessary to comply with sanitation requirements; or
(3) where a clean-up and resulting discharge is ordered and supervised by an appropriate governmental agency or court of competent jurisdiction.

§12705. Specific Regulatory Levels Posing No Significant Risk.
(a) Daily exposure to a chemical at a level which does not exceed the level set forth in subsections (b), (c) and (d) for such chemical shall be deemed to pose no significant risk within the meaning of Health and Safety Code section 25249.10 (c).
(b) Levels of exposure deemed to pose no significant risk may be determined by the lead agency based on a risk assessment conducted by the lead agency pursuant to the guidelines set forth in Section 12703, or a risk assessment reviewed by the lead agency and determined to be consistent with the guidelines set forth in Section 12703.
(1) The following levels based on risk assessments conducted or reviewed by the lead agency shall be deemed to pose no significant risk:

| Chemical Name | Level (micrograms/day) |
|---|---|
| Acrylonitrile | 0.7 |
| Aldrin | 0.04 |
| Arsenic | 0.06 (inhalation) |

| | |
|---|---|
| Asbestos | 100 fibers inhaled/day* |
| Benzene | 7 |
| Benzidine | 0.001 |
| Bis(2-chloroethyl)ether | 0.3 |
| Bis(chloromethyl)ether | 0.02 |
| Butylated hydroxyanisole | 4000 |
| Cadmium | 0.05 (inhalation) |
| Carbon tetrachloride | 5 |
| Chromium (hexavalent compounds) | 0.001 (inhalation) |
| DDT, DDE and DDD (in combination) | 2 |
| 1,2-Dibromo-3-chloropropane (DBCP) | 0.1 |
| para-Dichlorobenzene | 20 |
| 3,3'-Dichlorobenzidine | 0.6 |
| Dichloromethane (Methylene chloride) | 200 (inhalation) |
| Dieldrin | 0.04 |
| 1,4-Dioxane | 30 |
| Epichlorohydrin | 9 |
| Ethylene dibromide | 0.2 (ingestion)<br>3 (inhalation) |
| Ethylene dichloride | 10 |
| Ethylene oxide | 2 |
| Hexachlorobenzene | 0.4 |
| Hexachlorodibenzodioxin | 0.0002 |
| Hexachlorocyclohexane (technical grade) | 0.2 |
| N-Nitroso-n-dibutylamine | 0.06 |
| N-Nitrosodiethylamine | 0.02 |
| N-Nitrosodimethylamine | 0.04 |
| N-Nitrosodiphenylamine | 80 |
| N-Nitrosodi-n-propylamine | 0.1 |
| N-Nitroso-N-ethylurea | 0.03 |
| N-Nitroso-N-methylurea | 0.006 |
| Polybrominated biphenyls | 0.02 |
| 2,3,7,8-Tetrachlorodibenzo-p-dioxin | 0.000005 |
| Toxaphene | 0.6 |
| Trichloroethylene | 50 (ingestion)<br>80 (inhalation) |
| 2,4,6-Trichlorophenol | 10 |
| Urethane | 0.7 |
| Vinyl chloride | 3 |

*Fibers equal to or greater than 5 micrometers in length and 0.3 micrometers in width, with a length to width ratio of greater than or equal to 3:1 as measured by phase contrast microscopy.

(2) Whenever the lead agency proposes to formally adopt, pursuant to this subsection, a level which shall be deemed to pose no significant risk of cancer, assuming daily exposure at that level, the lead agency shall provide to each member of the Scientific Advisory Panel notice of the proposed action, a copy of the proposed level, and a copy of the initial statement of reasons supporting the proposal. The close of the public comment period for any such proposal shall be scheduled by the lead agency so as to permit the Scientific Advisory Panel the opportunity to review such proposal and provide comment to the lead agency. Any such comment by the Scientific Advisory Panel shall become a part of the formal rulemaking file. Nothing in this subsection shall be construed to prevent members of the Scientific Advisory Panel from providing comments individually on any such proposal, or to require the Scientific Advisory Panel to submit any comment.

(c) Unless a specific regulatory level for a chemical known to the state to cause cancer has been established in subsection (b), levels of exposure deemed to pose no significant risk may be determined by the lead agency based on state or federal risk assessments.

(1) Any interested party may request the lead agency to reevaluate a level established in this subsection based on scientific considerations that indicate the need for the lead agency to develop its own risk assessment or to conduct a detailed review of the risk assessment used to derive the level in question. Such request shall be made in writing, and shall include a description of the scientific considerations that indicate the need for the lead agency to develop its own risk assessment or to conduct a detailed review of the risk assessment used to derive the level in question. The lead agency may establish a level for the chemical in question in subsection (b) as it deems necessary.

(2) The following levels based on state or federal risk assessments shall be deemed to pose no significant risk:

| Chemical Name | Level (micrograms/day) |
|---|---|
| Acetaldehyde | 90 (inhalation) |
| Acrylamide | 0.2 |
| Allyl chloride | 30 |
| Aniline | 100 |
| Azobenzene | 6 |
| Benzo[a]pyrene | 0.06 |
| Benzyl chloride | 4 |
| Beryllium oxide | 0.1 |
| Beryllium sulfate | 0.0002 |
| Bromodichloromethane | 5 |
| 1,3-Butadiene | 0.4 |
| Chlordane | 0.5 |
| Chloroform | 20 (ingestion)<br>40 (inhalation) |
| Coke oven emissions | 0.3 |
| DDVP (Dichlorvos) | 2 |
| Dichloromethane (Methylene chloride) | 50 |
| Di(2-ethylhexyl)phthalate | 80 |
| 2,4-Dinitrotoluene | 2 |
| Folpet | 200 |
| Formaldehyde (gas) | 40 |
| Furmecyclox | 20 |
| Heptachlor | 0.2 |
| Heptachlor epoxide | 0.08 |
| Hexachlorocyclohexane | |
| alpha isomer | 0.3 |
| beta isomer | 0.5 |
| gamma isomer | 0.6 |
| Hydrazine | 0.04 |
| Hydrazine sulfate | 0.2 |
| 4,4'-Methylene bis (N,N-dimethyl)benzeneamine | 20 |
| Nickel refinery dust | 0.8 |
| Nickel subsulfide | 0.4 |
| N-Nitrosodiethanolamine | 0.3 |
| N-Nitrosomethylethylamine | 0.03 |
| N-Nitrosopyrrolidine | 0.3 |
| Pentachlorophenol | 40 |
| Polychlorinated biphenyls (PCBs) | 0.09 |
| Tetrachloroethylene | 14 |

(d) Unless a specific regulatory level has been established for a chemical known to the state to cause cancer in subsection (b) or (c), levels of exposure deemed to pose no significant risk may be determined by the lead agency using an expedited method consistent with the procedures specified in Section 12703.

(1) Any interested party may request the lead agency to reevaluate a level established in this subsection and to consider the adoption, in subsection (c), of a level based on a state or federal risk assessment. Such request shall be made in writing, and shall include a copy of the state or federal risk assessment which the interested party wishes the lead agency to consider as the basis for a level in subsection (c). The lead agency may establish a level in subsection (c) for the chemical in question based on a state or federal risk assessment as it deems necessary.

(2) Any interested party may request the lead agency to reevaluate a level established in this subsection based on scientific considerations that indicate the need for a conventional risk assessment. Such request shall be made in writing, and shall include a description of the scientific considerations that indicate the need for a conventional risk assessment. The lead agency may conduct a conventional risk assessment for the chemical in question, and establish a level in subsection (b) as it deems necessary.

(3) The following levels of exposure based on risk assessments conducted by the lead agency using an expedited method consistent with the procedures specified in Section 12703 shall be deemed to pose no significant risk:

| Chemical Name | Level (micrograms/day) |
|---|---|
| A-alpha-C (2-Amino-9H-pyridol[2,3-b]indole) | 2 |
| Acetamide | 10 |
| 2-Acetylaminofluorene | 0.2 |
| Actinomycin D | 0.00008 |
| AF-2;[2-(2-furyl)-3(5-nitro-2-furyl)] acrylamide | 3 |
| 2-Aminoanthraquinone | 20 |
| *o*-Aminoazotoluene | 0.2 |
| 4-Aminobiphenyl (4-aminodiphenyl) | 0.03 |
| 3-Amino-9-ethylcarbazole hydrochloride | 9 |
| l-Amino-2-methylanthraquinone | 5 |
| 2-Amino-5-(5-nitro-2-furyl) -1,3,4-thiadiazole | .04 |
| Amitrole | 0.7 |
| *o*-Anisidine | 5 |
| *o*-Anisidine hydrochloride | 7 |
| Aramite | 20 |
| Auramine | 0.8 |
| Azaserine | 0.06 |
| Azathioprine | 0.4 |
| Benzyl violet 4B | 30 |
| beta-Butyrolactone | 0.7 |
| Captafol | 5 |
| Captan | 300 |
| Chlorambucil | 0.002 |
| Chlordecone (Kepone) | 0.04 |
| Chlorendic acid | 8 |
| Chlorinated paraffins (Average chain length, C12; approximately 60 percent chlorine by weight) | 8 |
| Chlorodibromomethane | 7 |
| Chloromethyl methyl ether (technical grade) | 0.3 |
| 3-Chloro-2-methylpropene | 5 |
| 4-Chloro-ortho-phenylenediamine | 40 |
| Chlorothalonil | 200 |
| p-Chloro-o-toluidine | 3 |
| Chlorozotocin | 0.003 |

| | |
|---|---|
| C. I. Basic Red 9 monohydrochloride | 3 |
| Cinnamyl anthranilate | 200 |
| *p*-Cresidine | 5 |
| Cupferron | 3 |
| Cyclophosphamide (anhydrous) | 1 |
| Cyclophosphamide (hydrated) | 1 |
| D&C Red No. 9 | 100 |
| Dacarbazine | 0.01 |
| Daminozide | 40 |
| Dantron (Chrysazin; 1,8-Dihydroxyanthraquinone) | 9 |
| 2,4-Diaminoanisole | 30 |
| 2,4-Diaminoanisole sulfate | 50 |
| 4,4'-Diaminodiphenyl ether (4,4'-Oxydianiline) | 5 |
| 2,4-Diaminotoluene | 0.2 |
| Dibenz[a,h]anthracene | 0.2 |
| 1,1-Dichloroethane | 100 |
| Diethylstilbestrol | 0.002 |
| Digylcidyl resorcinol ether (DGRE) | 0.4 |
| Dihydrosafrole | 20 |
| 4-Dimethylaminoazobenzene | 0.2 |
| trans-2[Dimethylamino)methyliminol]-5-[2-(5-nitro-2-furyl)vinyl]- 1,3,4-oxadiazole | 2 |
| 7,12-Dimethylbenz(a)anthracene | 0.003 |
| Dimethylcarbamyl chloride | 0.05 |
| 1,2-Dimethylhydrazine | 0.001 |
| Dimethylvinylchloride | 20 |
| Direct Black 38 (technical grade) | 0.09 |
| Direct Blue 6 (technical grade) | 0.09 |
| Direct Brown 95 (technical grade) | 0.1 |
| Disperse Blue 1 | 200 |
| Estradiol 17B | 0.02 |
| Ethyl-4,4'-dichlorobenzilate (chlorobenzilate) | 7 |
| Ethylene thiourea | 20 |
| Ethyleneimine | 0.01 |
| 2-(2-Formylhydrazino)-4-(5-nitro-2- furyl)thiazole | 0.3 |
| Glu-P-1 (2-Amino-6-methyldipyrido[1,2-a:3',2'-d]imidazole) | 0.1 |
| Glu-P-2 (2-Aminodipyrido[1,2-a:3',2'-d]imidazole | 0.5 |
| Gyromitrin (Acetaldehyde methylformylhydrazone) | 0.07 |
| HC Blue 1 | 10 |
| Hexachloroethane | 20 |
| Hydrazobenzene (1,2-Diphenylhydrazine) | 0.8 |
| IQ (2-Amino-3-methylimidazo[4,5-f]quinoline] | 0.5 |
| Lasiocarpine | 0.09 |
| Lead acetate | 3 |
| Lead subacetate | 20 |
| Me-A-alpha-C (2-Amino-3-methyl-9H-pyrido[2,3-b]indole) | 0.6 |
| Melphalan | 0.005 |
| 3-Methylcholanthrene | 0.03 |
| 4,4'-Methylene bis(2-chloroaniline) | 0.5 |
| 4,4'-Methylene bis(2-methylaniline) | 0.8 |
| 4,4'-Methylenedianiline | 0.4 |
| 4,4'-Methylenedianiline dihydrochloride | 0.6 |
| Methyl methanesulfonate | 7 |
| 2-Methyl-1-nitroanthraquinone (of uncertain purity) | 0.2 |
| N-Methyl-N'-nitro-N-nitrosoguanidine | 0.08 |
| Methylthiouracil | 2 |

| | |
|---|---|
| Michler's ketone | 0.8 |
| Mirex | 0.04 |
| Mitomycin C | 0.00009 |
| Monocrotaline | 0.07 |
| 2-Naphthylamine | 0.4 |
| Nitrilotriacetic acid | 100 |
| Nitrilotriacetic acid, trisodium salt monohydrate | 70 |
| 5-Nitroacenaphthene | 6 |
| 5-Nitro-o-anisidine | 10 |
| Nitrofen (technical grade) | 9 |
| Nitrofurazone | 0.5 |
| 1-[5-Nitrofurfurylidine)-amino]-2-imidazolidinone | 0.4 |
| N-[4-(5-Nitro-2-furyl)-2-thiazolyl] acetamide | 0.5 |
| p-Nitrosodiphenylamine | 30 |
| N-Nitroso-N-methylurethane | 0.006 |
| N-Nitrosomorpholine | 0.1 |
| N-Nitrosonornicotine | 0.5 |
| N-Nitrosopiperidine | 0.07 |
| Phenacetin | 300 |
| Phenazopyridine | 4 |
| Phenazopyridine hydrochloride | 5 |
| Phenesterin | 0.005 |
| Phenobarbital | 2 |
| Phenoxybenzamine | 0.2 |
| Phenoxybenzamine hydrochloride | 0.3 |
| o-Phenylphenate, sodium | 200 |
| Ponceau MC (D&C Red No. 5) | 200 |
| Ponceau 3R (FD&C Red No. 1) | 40 |
| Potassium bromate | 1 |
| Procarbazine | 0.05 |
| Procarbazine hydrochloride | 0.06 |
| 1,3-Propane sultone | 0.3 |
| beta-Propiolactone | 0.05 |
| Propylthiouracil | 0.7 |
| Reserpine | 0.06 |
| Safrole | 3 |
| Sterigmatocystin | 0.02 |
| Streptozotocin | 0.006 |
| Styrene oxide | 4 |
| Sulfallate | 4 |
| 1,1,2,2-Tetrachloroethane | 3 |
| Thiocetamide | 0.1 |
| 4,4'-Thiodianiline | 0.05 |
| Thiourea | 10 |
| Toluene diisocyanate | 20 |
| *o*-Toluidine | 4 |
| *o*-Toluidine hydrochloride | 5 |
| Tris(1-aziridinyl)phosphine sulfide (Thiotepa) | 0.06 |
| Tris(2,3-dibromopropyl)phosphate | 0.3 |
| Trp-P-1 (Tryptophan-P-1) | 0.03 |
| Trp-P-2 (Tryptophan-P-2) | 0.2 |
| Vinyl trichloride (1,1,2-Trichloroethane) | 10 |

§12707. Routes of Exposure.

(a) Where scientifically valid absorption studies conducted according to generally accepted standards demonstrate that absorption of a chemical through a specific route of exposure can be reasonably

anticipated to present no significant risk of cancer at levels of exposure not in excess of current regulatory levels, the lead agency may identify the chemical as presenting no significant risk by that route of exposure. Any exposure, discharge or release of a chemical so identified shall be deemed to present no significant risk to the extent that it results in exposure to humans by the identified route, and does not exceed the level established in any other applicable federal or state standard, regulation, guideline, action level, license, permit, condition, requirement or order.

(b) The following chemicals present no significant risk of cancer by the route of ingestion:
(1) Asbestos
(2) Beryllium and beryllium compounds
(3) Cadmium and cadmium compounds
(4) Chromium (hexavalent compounds)
(5) Nickel and nickel compounds

§12709. Exposure to Trace Elements.

(a) Except where a specific regulatory level is established in Section 12705, exposure to a trace element listed in (b) shall be deemed to pose no significant cancer risk so long as the reasonably anticipated level of exposure to the chemical does not exceed the level set forth in (b).

| (b) Element | No Significant Risk Level in micrograms per day |
|---|---|
| Arsenic (inorganic) | 10 (except inhalation) |
| Beryllium | 0.1 |

§12711. Levels Based on State or Federal Standards.

(a) Except as otherwise provided in section 12705, 12707, 12709, or 12713, levels of exposure deemed to pose no significant risk may be determined as follows:
(1) Where a state or federal agency has developed a regulatory level for a chemical known to the state to cause cancer which is calculated to result in not more than one excess case of cancer in an exposed population of 100,000, such level shall constitute the no significant risk level.
(2) For drinking water, the following levels shall be deemed to pose no significant risk:
(A) Drinking water maximum contaminant levels adopted by the Department of Health Services for chemicals known to the state to cause cancer;
(B) Drinking water action levels for chemicals known to the state to cause cancer for which maximum contaminant levels have not been adopted;
(C) Specific numeric levels of concentration for chemicals known to the state to cause cancer which are permitted to be discharged or released into sources of drinking water by a Regional Water Quality Control Board in a water quality control plan or in waste discharge requirements, when such levels are based on considerations of minimizing carcinogenic risks associated with such discharge or release.

## Article 8. No Observable Effect Levels

§12801. General.

(a) The determination of whether a level of exposure to a chemical known to the state to cause reproductive toxicity has no observable effect for purposes of Health and Safety Code Section 25249.10(c) shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of a chemical as known to the state to cause reproductive toxicity. Nothing in this article shall preclude a person from using evidence, standards, assessment methodologies, principles, assumptions or levels not described in this article to establish that a level of exposure has no observable effect at one thousand (1,000) times the level in question.

(b) A level of exposure to a listed chemical shall be deemed to have no observable effect, assuming exposure at one thousand times that level, provided that the level is determined:
(1) By means of an assessment that meets the standards described in section 12803 to determine the maximum dose level having no observable effect, and dividing that level by one thousand (1,000) to arrive at the maximum allowable dose level; or

(2) By application of a specific regulatory level for the chemical in question as provided in Section 12805.

(c) For purposes of this article, "NOEL" shall mean that no observable effect level, which is the maximum dose level at which a chemical has no observable reproductive effect.

(d) The chemicals specifically contained in this article do not include all listed reproductive toxicants for which there is a level of exposure which has no observable effect assuming exposure at one thousand times the level in question. The fact that a chemical does not specifically appear in this article does not mean that it has an observable effect at any level.

(e) This article establishes exposure levels solely for purposes of Health and Safety Code Section 25249.10(c). Nothing in this article shall be construed to establish exposure levels for other regulatory purposes.

§12803. Assessment.

(a) A quantitative risk assessment which conforms to this section shall be deemed to determine the level of exposure to a listed chemical which has no observable effect, assuming exposure at one thousand times the level in question. The assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause reproductive toxicity. In the absence of principles or assumptions scientifically more appropriate, based upon the available data, the following default principles and assumptions shall apply in any such assessment:

(1) Only studies producing the reproductive effect which provides the basis for the determination that a chemical is known to the state to cause reproductive toxicity shall be utilized for the determination of the NOEL. Where multiple reproductive effects provide the basis for the determination that a chemical is known to the state to cause reproductive toxicity, the reproductive effect for which studies produce the lowest NOEL shall be utilized for the determination of the NOEL. The NOEL shall be the highest dose level which results in no observable reproductive effect, expressed in milligrams of chemical per kilogram of bodyweight per day.

(2) The quality and suitability of available epidemiologic data shall be appraised to determine whether the study is appropriate as the basis of an assessment considering such factors as the selection of the exposed and reference groups, the reliable ascertainment of exposure, and completeness of follow-up. Biases and confounding factors shall be identified and quantified.

(3) Animal bioassay studies for assessment shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, and the route of exposure and the extent of occurrence of effects.

(4) The NOEL shall be based on the most sensitive study deemed to be of sufficient quality.

(5) The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.

(6) When available data are of such quality that anatomic, physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the assessment.

(7) When data do not allow the determination of a NOEL, the lowest observable effect level (LOEL) shall be divided by 10 to establish a NOEL for purposes of assessment.

(b) The NOEL shall be converted to a milligram per day dose level by multiplying the assumed human body weight by the NOEL. When the applicable reproductive effect is upon the male, human body weight of 70 kilograms shall be assumed. When the applicable reproductive effect is upon the female or conceptus, human body weight of 58 kilograms shall be assumed.

§12805. Specific Regulatory Levels: Reproductive Toxicants.

(a) Exposure to a chemical at a level which does not exceed the level set forth in subsection (b) for such chemical has no observable effect assuming exposure at one thousand (1,000) times that level.

| (b) Chemical Name | Level (Micrograms/day) |
|---|---|
| Ethylene Oxide | 20.0 |
| Lead | 0.5 |
| Toluene | 7000 |

(c) Unless a specific level is otherwise provided in this section, an assessment by an agency of the state or federal government that is the substantial equivalent of the assessment described in subdivision (a) of Section 12803, and establishes a maximum allowable daily dose level in the manner provided in paragraph (b)(1) of Section 12801, shall constitute the allowable daily dose level having no observable effect within the meaning of Health and Safety Code Section 25249.10(c).